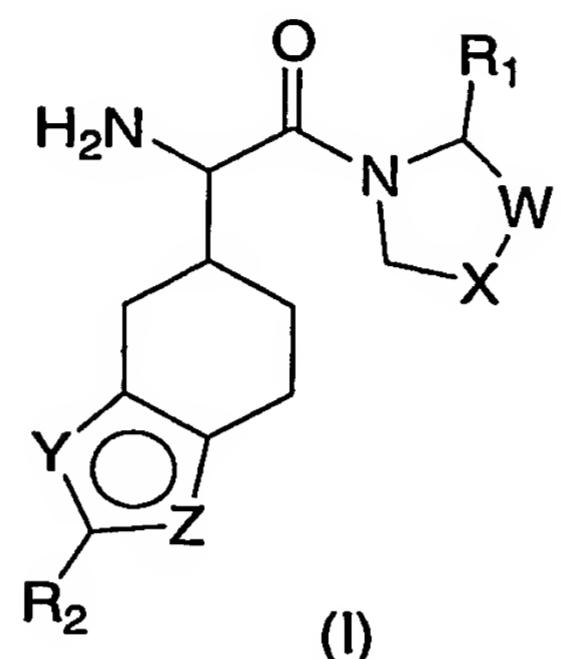


## WHAT IS CLAIMED IS:

## 1. A compound of structural formula I:



5 wherein:

each n is independently 0, 1, 2, or 3;

W is selected from the group consisting of CH<sub>2</sub>, CHF, and CF<sub>2</sub>;10 X is selected from the group consisting of S, S(O), S(O)<sub>2</sub>, CH<sub>2</sub>, CHF, and CF<sub>2</sub>;Y and Z are each independently selected from the group consisting of O, S, N, and NR<sup>7</sup>, with the proviso that at least one of Y and Z is N;15 R<sup>1</sup> is hydrogen or cyano;R<sup>2</sup> is selected from the group consisting of

hydrogen,

halogen,

20 cyano,

hydroxy,

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,C<sub>1-6</sub> alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,(CH<sub>2</sub>)<sub>n</sub>-COOH,25 (CH<sub>2</sub>)<sub>n</sub>-COOC<sub>1-6</sub> alkyl,(CH<sub>2</sub>)<sub>n</sub>-CONR<sup>3</sup>R<sup>4</sup>,(CH<sub>2</sub>)<sub>n</sub>-NR<sup>3</sup>R<sup>4</sup>,

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>6</sup>SO<sub>2</sub>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>6</sup>CONR<sup>3</sup>R<sup>4</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>6</sup>COR<sup>6</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>6</sup>CO<sub>2</sub>R<sup>5</sup>,

5 (CH<sub>2</sub>)<sub>n</sub>-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO<sub>2</sub>H, C<sub>1</sub>-6 alkyloxycarbonyl, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>2</sup> is independently unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1</sub>-4 alkyl unsubstituted or substituted with one to five halogens;

10 R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen,

15 (CH<sub>2</sub>)<sub>n</sub>-phenyl,  
(CH<sub>2</sub>)<sub>n</sub>-C<sub>3</sub>-6 cycloalkyl, and  
C<sub>1</sub>-6 alkyl,

20 wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; or

25 R<sup>3</sup> and R<sup>4</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and  
C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

30 each R<sup>5</sup> is independently selected from the group consisting of (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>5</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1</sub>-4 alkyl unsubstituted or substituted with one to five halogens;

each R<sup>6</sup> is hydrogen or R<sup>5</sup>; and

$R^7$  is selected from the group consisting of

hydrogen.

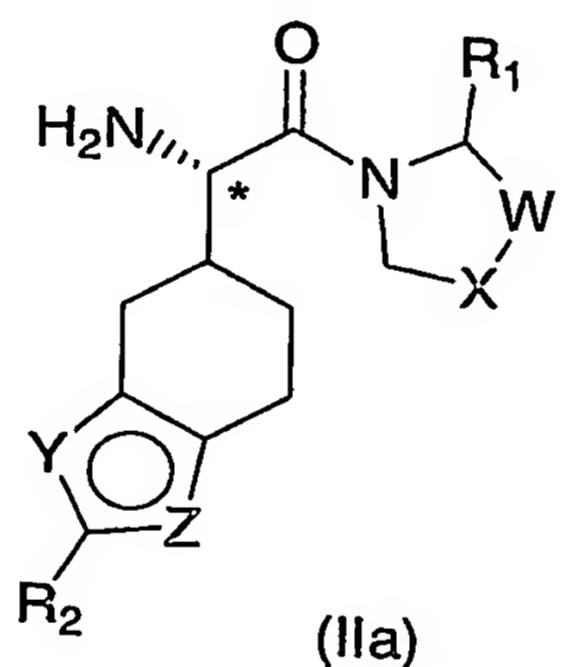
(CH<sub>2</sub>)<sub>n</sub>-phenyl.

(CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and

C<sub>1-6</sub> alkyl,

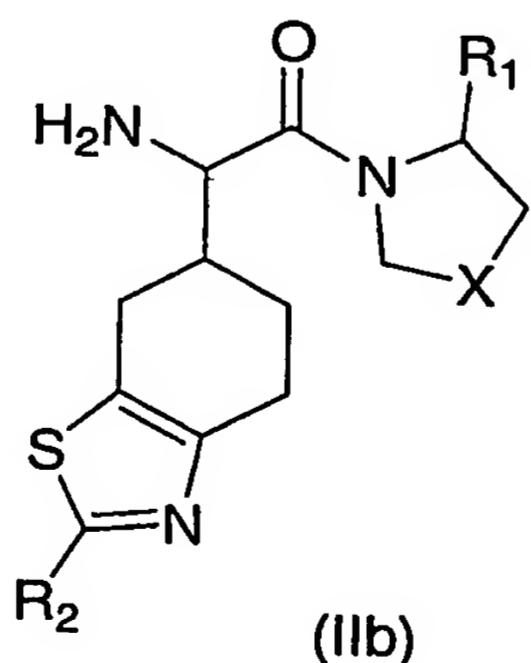
wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens.

2. The compound of Claim 1 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula IIa:



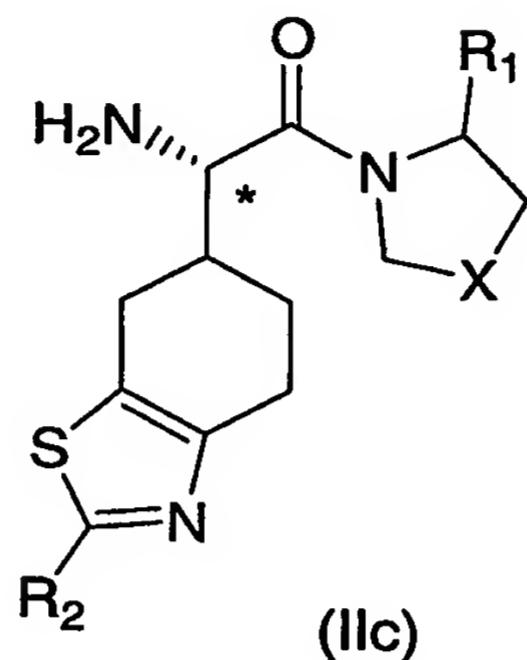
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3. The compound of Claim 1 of structural formula IIb:



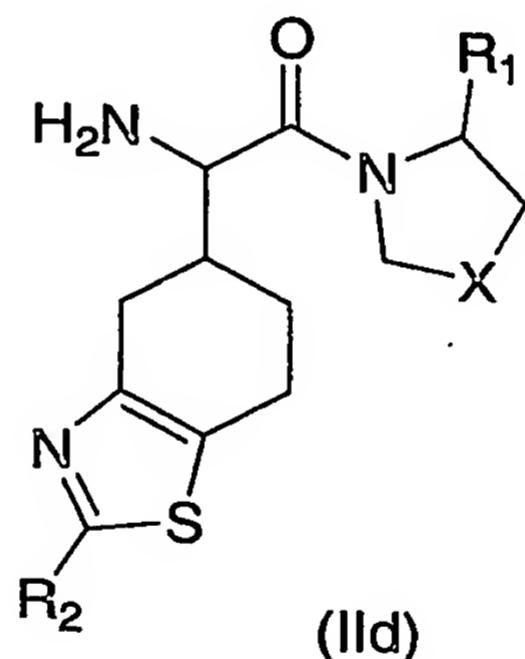
4. The compound of Claim 3 wherein X is  $\text{CH}_2$ ,  $\text{CHF}$ , or  $\text{CF}_2$  and  $\text{R}^1$  is hydrogen.

5. The compound of Claim 3 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula IIc:



5 and wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

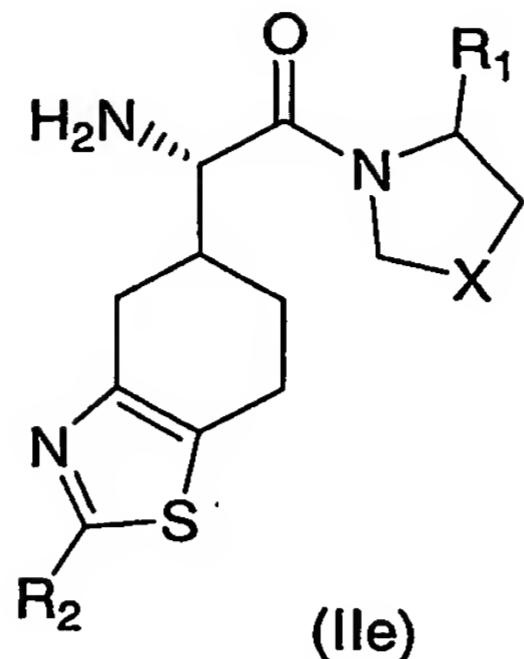
6. The compound of Claim 1 of structural formula Id:



7. The compound of Claim 6 wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

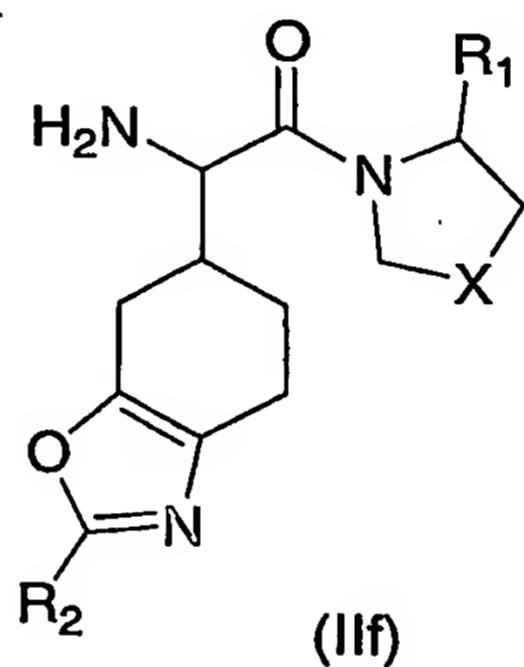
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8. The compound of Claim 6 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula IIe:



wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

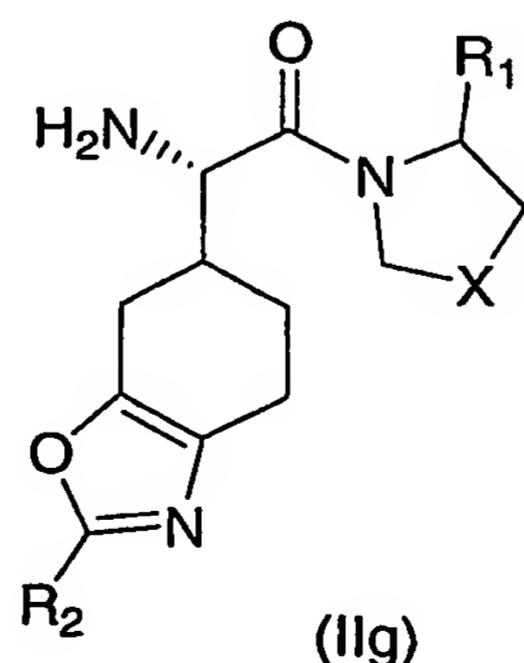
9. The compound of Claim 1 of structural formula IIf:



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10. The compound of Claim 9 wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

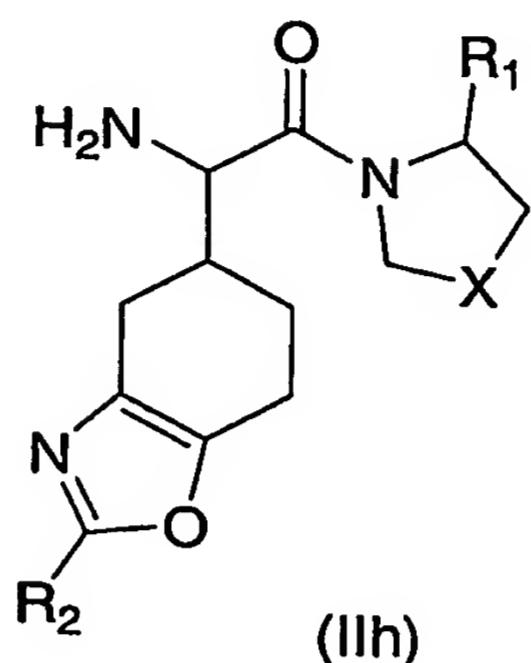
11. The compound of Claim 9 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula IIg:



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wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

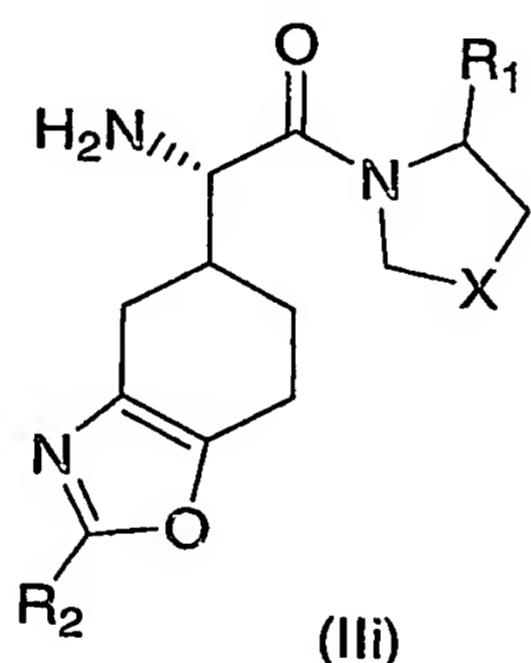
12. The compound of Claim 1 of structural formula IIIh:



13. The compound of Claim 12 wherein X is  $\text{CH}_2$ ,  $\text{CHF}$ , or  $\text{CF}_2$  and  $\text{R}^1$  is hydrogen.

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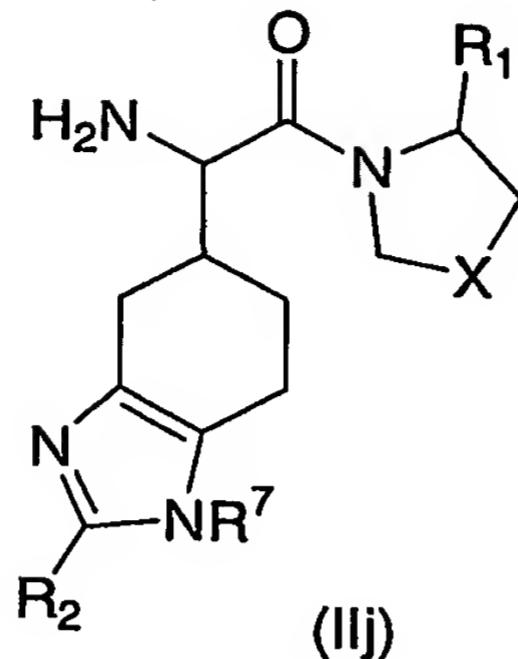
14. The compound of Claim 12 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula IIIi:



wherein X is  $\text{CH}_2$ ,  $\text{CHF}$ , or  $\text{CF}_2$  and  $\text{R}^1$  is hydrogen.

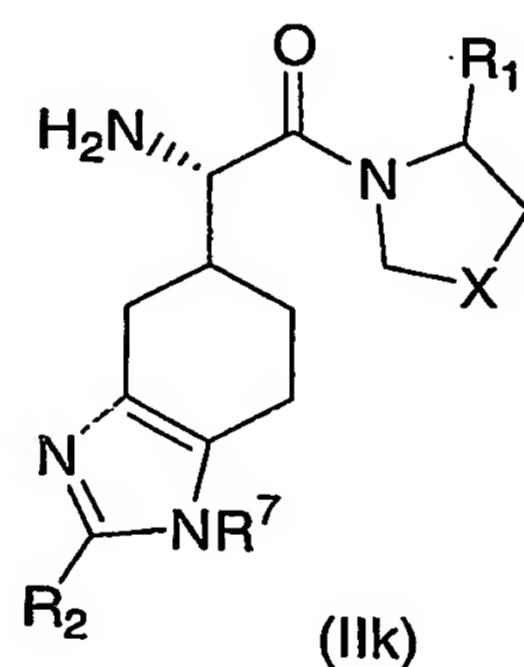
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15. The compound of Claim 1 of structural formula IIj:



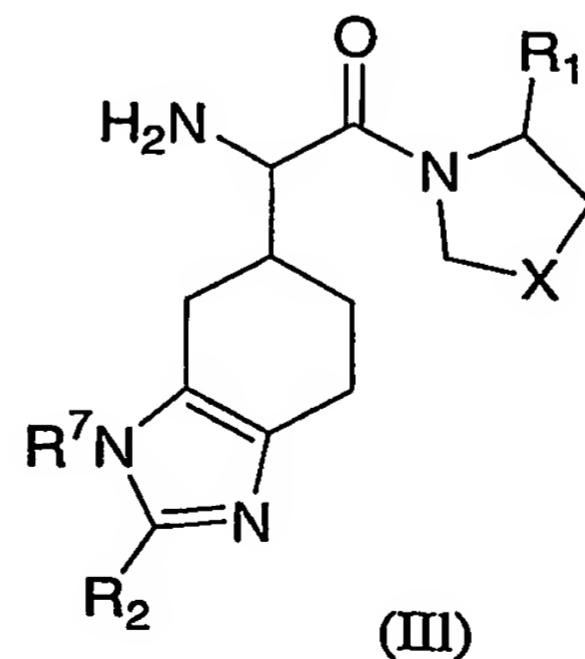
16. The compound of Claim 15 wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

17. The compound of Claim 15 wherein the carbon atom marked with an \* has the  
5 stereochemical configuration as depicted in formula IIIk:



wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

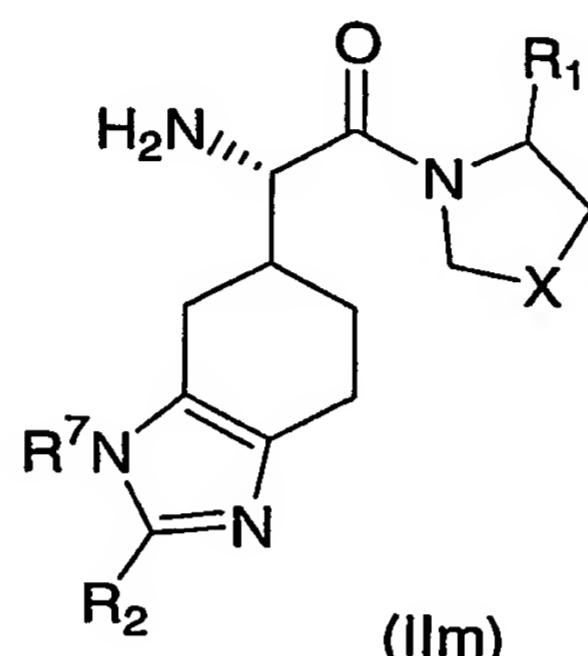
18. The compound of Claim 1 of structural formula III:



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19. The compound of Claim 18 wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

20. The compound of Claim 18 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula II<sup>m</sup>:



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wherein X is CH<sub>2</sub>, CHF, or CF<sub>2</sub> and R<sup>1</sup> is hydrogen.

21. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

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22. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15 23. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 24. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

25 25. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

26. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a

mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

27. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

28. The pharmaceutical composition of Claim 21 further comprising one or more additional active ingredients selected from the group consisting of:

- (a) a second dipeptidyl peptidase IV inhibitor;
- (b) an insulin sensitizer selected from the group consisting of a PPAR $\gamma$  agonist, a PPAR $\alpha/\gamma$  dual agonist, a PPAR $\alpha$  agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;
- (c) an insulin or insulin mimetic;
- (d) a sulfonylurea or other insulin secretagogue;
- (e) an  $\alpha$ -glucosidase inhibitor;
- (f) a glucagon receptor antagonist;
- (g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
- (h) GIP, a GIP mimetic, or a GIP receptor agonist;
- (i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;
- (j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPAR $\alpha$  agonist, (v) PPAR $\alpha/\gamma$  dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and (viii) anti-oxidant;
- (k) a PPAR $\delta$  agonist;
- (l) an antiobesity compound;
- (m) an ileal bile acid transporter inhibitor;
- (n) an anti-inflammatory agent; and

(o) an antihypertensive agent.

29. The pharmaceutical composition of Claim 28 wherein the PPAR $\alpha/\gamma$  dual agonist is KRP-297.

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30. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR $\alpha/\gamma$  dual agonist KRP-297.

10 31. A method of controlling or treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer or an insulin secretagogue.